

Dynamics and optimal control of Ebola transmission

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Abstract A major Ebola outbreak occurs in West Africa since March 2014, being the deadliest epidemic in history. As an infectious disease epidemiology, Ebola is the most lethal and is moving faster than in previous outbreaks. On 8 August 2014, the World Health Organization (WHO) declared the outbreak a public health emergency of international concern. Last update on 7 July 2015 by WHO reports 27 609 cases of Ebola with a total of 11 261 deaths. In this work, we present a mathematical description of the spread of Ebola virus based on the SEIR (Susceptible–Exposed–Infective–Recovered) model and optimal strategies for Ebola control. In order to control the propagation of the virus and to predict the impact of vaccine programmes, we investigate several strategies of optimal control of the spread of Ebola: control infection by vaccination of susceptible; minimize exposed and infected; reduce Ebola infection by vaccination and education.

Keywords Mathematical modelling · optimal control · epidemiology · Ebola virus · 2014 Ebola epidemic in West Africa.

1 Introduction

The most widespread epidemic of Ebola virus disease in history is currently ongoing in West Africa. Ebola virus is the most complex and lethal pathogen

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for humans [7, 19]. The first outbreak was in 1976 in Congo, close to Ebola river, where the disease takes its name. The Ebola virus causes an acute, often fatal haemorrhagic illness. The current outbreak in West Africa is the largest and most complex Ebola outbreak since the virus discovery. The increasing of this virulent virus is extremely rapid and has evolved into a health and humanitarian catastrophe of historic scope. The incubation period, that is, the time interval from infection with the virus to the onset of symptoms, is 2 to 21 days. Humans are not infectious to another person until they develop symptoms. Symptoms typically begin with sudden onset of fever, sore throat, muscle pain, and headaches. Then, vomiting, diarrhoea and rash usually follow, along with decreased function of the liver and kidneys. At this time infectious individuals begin to bleed, both internally and externally (bleeding from nose, mouth, eyes and anus). In final stage, these symptoms are followed by death [10, 13, 18, 20, 24, 31, 33]. Ebola spreads through human-to-human transmission via close and direct physical contact (through broken skin or mucous membranes) with infected bodily fluids. The most infectious fluids are blood, faeces and vomit secretions; however, all body fluids have the capacity to transmit the virus. The virus is also transmitted indirectly via exposure to objects or environment contaminated with infected secretions. Because of this, healthcare workers must practice strict infection prevention and control precautions.

In epidemiology, mathematical models are a key tool that contribute to the understanding of the dynamics of a virus and the impact of vaccination programmes. More precisely, Mathematics has an important role in the study of propagation of virus spreads by allowing policy-makers to predict the impact of particular vaccine programmes or to derive more efficient strategies based on mathematical insights [26, 29]. In recent years, optimal control theory has become a powerful mathematical tool to assess the intervention of public health authorities. Indeed, the inclusion, in an epidemic model, of some practical control strategies, like vaccines, social distancing or quarantine, provides a rational basis for policies designed to control the spread of the virus. In this spirit, the aim of this work is to investigate effective strategies to control the spread of the Ebola virus by setting appropriate optimal control problems subject to a SEIR epidemic model that divides the population into four groups: the Susceptible, the Exposed (infected but not infectious), the Infectious, and the Recovered [1, 5, 11, 12, 35]. For a comparison study between the SIR and SEIR models we refer the reader to [23]. The main practical strategy of optimal control adopted is a vaccine [6, 8, 14, 16, 30]. For fractional (non-integer order) models see [2, 3].

The paper is organized as follows. In Section 2 we present the mathematical model that describes the dynamics of the spread of Ebola virus in West Africa. In Section 3 we study several control strategies for the propagation of the virus by using the proposed model. In these strategies, we use parameters estimated from recent statistical data based on the WHO report of the 2014 Ebola outbreak [34]. In Sections 3.1 and 3.2 we study the case of control through vaccination treatment by considering two different objective functions. In Section 3.3 we consider educational campaigns as a control, coupled with the

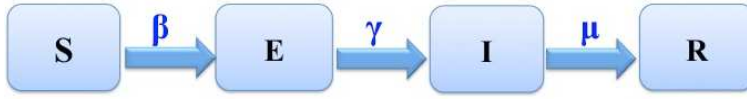


Fig. 1 Compartment diagram of the Susceptible–Exposed–Infectious–Recovered (SEIR) model (2).

vaccination treatment. We end with Section 4 of discussion of the numerical results and with Section 5 of conclusions and future work.

2 The basic model equations

In this section, we describe the transmission of Ebola virus by a SEIR model, where the population is divided into four groups: the susceptible individuals at time t , denoted by $S(t)$, enter the exposed class $E(t)$ before they become infectious. The infectious class at time t , denoted by $I(t)$, represents the individuals that are infected with the disease and are suffering the symptoms of Ebola. Finally, we have the recovered class, which at time t is denoted by $R(t)$. The total population, assumed constant during the short period of time under study, is given by

$$N = S(t) + E(t) + I(t) + R(t) \quad (1)$$

at any instant of time t . The transmission of Ebola virus is then described by the following set of nonlinear ordinary differential equations (ODEs):

$$\begin{cases} \frac{dS(t)}{dt} = -\beta S(t)I(t), \\ \frac{dE(t)}{dt} = \beta S(t)I(t) - \gamma E(t), \\ \frac{dI(t)}{dt} = \gamma E(t) - \mu I(t), \\ \frac{dR(t)}{dt} = \mu I(t). \end{cases} \quad (2)$$

Transitions between different states are described by the following parameters:

- the transmission rate β ,
- the infectious rate γ ,
- the recovered rate μ .

Figure 1 shows the relationship between the variables of model (2). Its numerical resolution is studied by Rachah and Torres in [22]. See also [21] for a simpler SIR model describing Ebola.

Remark 1 The model we consider here is very simple and assumes that the population is constant in the period of time under study: the sum of the right-hand side of the equations of system (2) is zero. The possibility to design more

complex models for a non-constant population is possible: see the recent eight state-variables model of [3]. However, for the analysis and simulation of the model to be possible, the authors of [3] imposed conditions to maintain the population N constant. As remarked at the end of [3], the design of strategies when the population is not constant seems to be a good topic of research.

3 Strategies for the control of the virus

Recently, epidemiological models have used optimal control techniques. Most works focus on HIV, tuberculosis (TB) and dengue [8, 14, 25, 26, 28, 29]. Control efforts are carried out to limit the spread of the disease and, in some cases, to prevent the emergence of drug resistance. In this section, we formulate several optimal control problems subject to the SEIR model (2), in order to derive the optimal treatment strategies. For each strategy, we study a specific objective in order to minimize not only the number of infected individuals and the systemic costs of treatments, but also to include an educational campaign with the vaccination treatment. The integration of educational campaigns has a great importance in countries that do not have the capacity to defend themselves against the virus. We compare the result of each strategy with the simulation results previously studied by Rachah and Torres in [22], the so called Strategy 1, which is described in Section 3.1. Strategies 2 and 3 are an improvement of the Strategy 1 of [22], and are given in Sections 3.2 and 3.3, respectively. More precisely, Strategy 3 consists in the study of an educational campaign (about the virus) coupled with a vaccination treatment. A comparison between the different strategies and the simulation results is given in Section 4.

Two approaches are common in optimal control: direct and indirect methods [27]. The direct methods are based in the discretization of the optimal control problems, reducing them to nonlinear constrained optimization problems. Indirect methods are based on the Hamiltonian and the Pontryagin maximum principle. In this work we have adopted the direct approach. We have computed the numerical solutions of the optimal control problems with the help of the ACADO solver [4]. ACADO is based on a multiple shooting method, including automatic differentiation and based ultimately on the semidirect multiple shooting algorithm of Bock and Pitt [9]. The ACADO solver comes as a self-contained public domain software environment, written in C++, for automatic control and dynamic optimization. The reader interested in the details of the implemented algorithms is referred to [15].

3.1 Strategy 1

In this subsection, we present the optimal control problem investigated in [22], obtained by introducing into the model (2) a control $u(t)$ representing the vaccination rate at time t . The control $u(t)$ is the fraction of susceptible individuals being vaccinated per unit of time. Then, the mathematical model

with control is given by the following system of nonlinear differential equations:

$$\begin{cases} \frac{dS(t)}{dt} = -\beta S(t)I(t) - u(t)S(t), \\ \frac{dE(t)}{dt} = \beta S(t)I(t) - \gamma E(t), \\ \frac{dI(t)}{dt} = \gamma E(t) - \mu I(t), \\ \frac{dR(t)}{dt} = \mu I(t) + u(t)S(t). \end{cases} \quad (3)$$

The goal of the strategy is to reduce the infected individuals and the cost of vaccination. Precisely, the optimal control problem consists of minimizing the objective functional

$$J(u) = \int_0^{t_{end}} \left[I(t) + \frac{\tau}{2} u^2(t) \right] dt, \quad (4)$$

where $u(t)$ is the control variable, which represents the vaccination rate at time t , and the positive parameters τ and t_{end} denote, respectively, the weight on cost and the duration of the vaccination program.

3.2 Strategy 2

We now improve the strategy of Section 3.1 by studying other strategy in order to better control the propagation of the spread of Ebola into populations. Our goal in this strategy is to reduce the number of exposed and infected individuals. More precisely, our optimal control problem consists of minimizing the objective functional

$$J(u) = \int_0^{t_{end}} \left[A_1 E(t) + A_2 I(t) + \frac{\nu}{2} u^2(t) \right] dt \quad (5)$$

subject to the model described by (3). The two first terms in the functional objective (5) represent benefit of $E(t)$ and $I(t)$ populations that we wish to reduce; A_1 and A_2 are positive constants to keep a balance in the size of $E(t)$ and $I(t)$, respectively. In the quadratic term of (5), ν is a positive weight parameter associated with the control $u(t)$, and the square of the control variable reflects the severity of the side effects of the vaccination. One has $u \in \mathcal{U}_{ad}$, where

$$\mathcal{U}_{ad} = \{u : u \text{ is measurable}, 0 \leq u(t) \leq u_{max} < \infty, t \in [0, t_{end}]\}$$

is the admissible control set, with $u_{max} = 0.9$. Note that it is not realistic to admit the possibility to vaccinate everybody and the value 0.9 means that, at maximum, 90% of susceptible are vaccinated. In the numerical simulations of model (2) and Strategy 1 of optimal control, Rachah and Torres [22] used

the parameters estimated on November 2014 by Althaus and Kaurov [1,17], who studied statistically the data of the World Health Organisation (WHO) [34]. In particular, in the statistical study [17], Kaurov studies the outbreak by modeling it with Wolfram's *Mathematica* language.

In order to compare our improvement of the optimal control study with the previous results of [22], we use here the same parameters, that is, the same rate of infection $\beta = 0.2$, the infectious rate $\gamma = 0.1887$, the same recovered rate $\mu = 0.1$, and the same initial values $(S(0), E(0), I(0), R(0)) = (0.88, 0.07, 0.05, 0)$ for the initial number of susceptible, exposed, infected, and recovered populations (at the beginning, 88% of population is susceptible, 7% is exposed and 5% is infected with Ebola). Figures 2, 3, 4 and 5 show, respectively, the significant difference in the number of susceptible, recovered, exposed and infected individuals with Strategy 1, Strategy 2, and without control. In Figure 2, we see that the number of susceptible S , in case of optimal control under Strategy 2, decreases more rapidly during the vaccination campaign. It reaches 2% at the end of the campaign, in contrast with the 6.6% at the end of the campaign with Strategy 1, and against 17.3% in the absence of optimal control. Figure 3 shows that the number of recovered individuals increases rapidly. The number $R(t_{end})$ at the end of the optimal control vaccination period of Strategy 2 is 97.9%, instead of 93.3% in case of Strategy 1, and against 81.2% without control. Figure 4 presents the time-dependent curve of exposed individuals. This curve shows that there is no peak of the curve of exposed individuals in case of control with Strategy 1 and Strategy 2 when we compare it with the curve in case without control, which shows a high peak. When we compare Strategy 1 and Strategy 2, we see that the curve of exposed individuals decreases more rapidly in case of control with Strategy 2. The period of incubation of the virus is only 30 days in case of control with Strategy 2 instead of 50 days in Strategy 1. In Figure 5, the time-dependent curve of infected individuals shows that the peak of the curve of infected individuals is less important in case of control with Strategy 2. In fact, the maximum value on the infected curve I under optimal control is 7% in case of Strategy 2, instead of 7.56% in Strategy 1, and against 14% without any control (see Figure 5). The other important effect of Strategy 2, which we see in the same curve, is the period of infection, which is the less important. The value of the period of infection is 65 days in case of Strategy 2, instead of 80 days in case of Strategy 1, and against more than 100 days without vaccination. This shows the efficiency of vaccination with Strategy 2 in controlling Ebola. Figure 6 gives a representation of the optimal control $u(t)$ for Strategy 1 and Strategy 2. The minimum values of the $J(u)$ functionals (4) and (5) are, respectively, 1,936 (Strategy 1) and 2,509 (Strategy 2).

3.3 Strategy 3

In this strategy we use the fact that individuals can acquire immunity against the virus either through educational campaigns or recovery after treatment

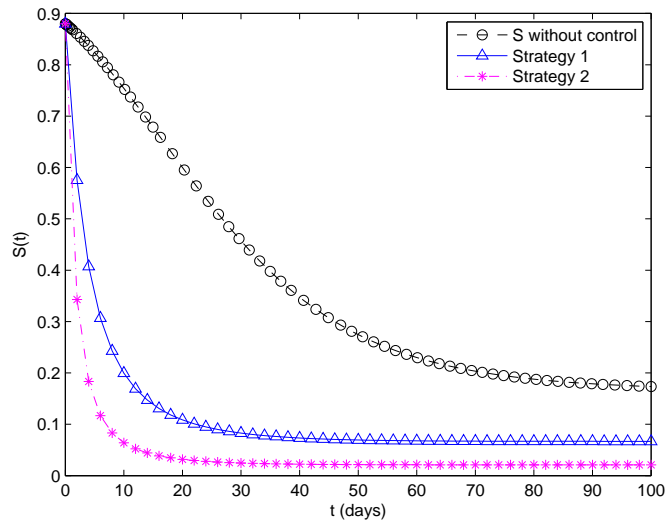


Fig. 2 Comparison between the curves of susceptible individuals $S(t)$ in case of Strategy 1 and Strategy 2 *versus* without control.

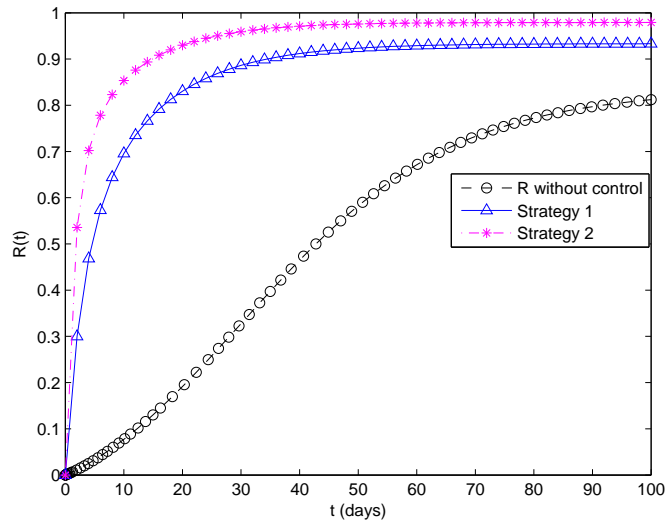


Fig. 3 Comparison between the curves of recovered individuals $R(t)$ in case of Strategy 1 and Strategy 2 *versus* without control.

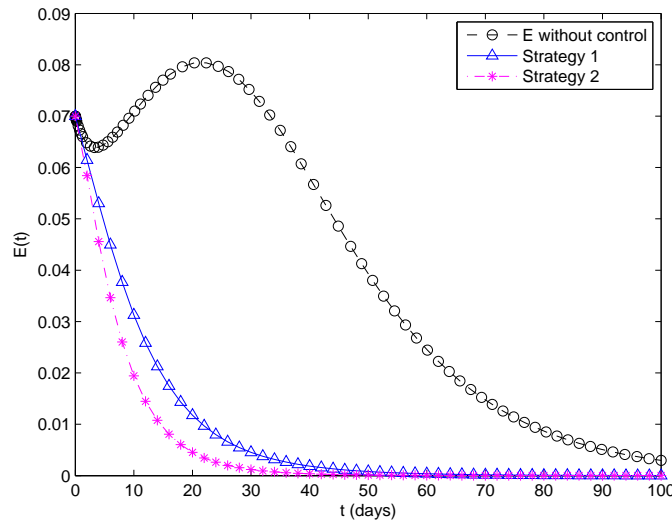


Fig. 4 Comparison between the curves of exposed individuals $E(t)$ in case of Strategy 1 and Strategy 2 *versus* without control.

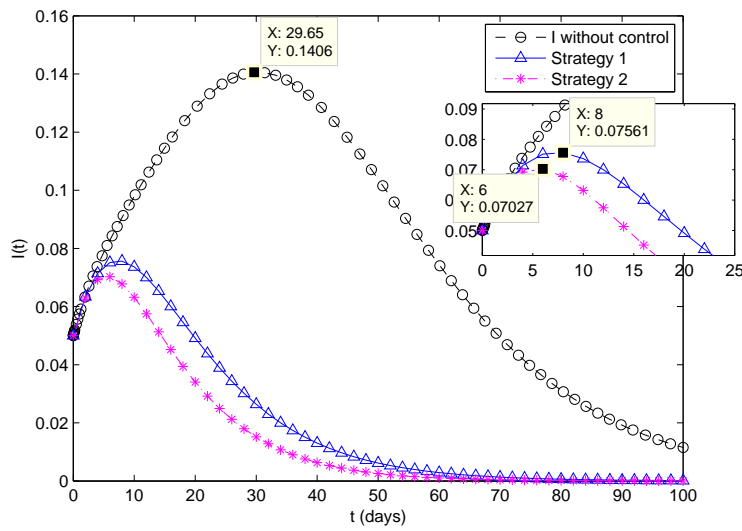


Fig. 5 Comparison between the curves of infected individuals $I(t)$ in case of Strategy 1 and Strategy 2 *versus* without control.

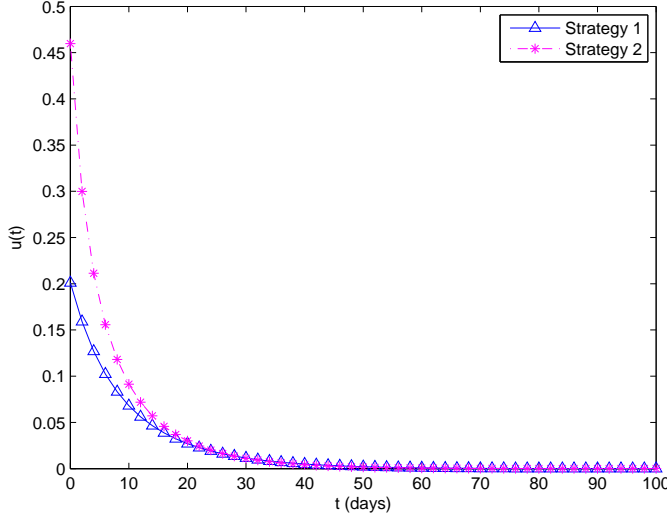


Fig. 6 The optimal control u for Strategy 1 and Strategy 2.

for the virus. Our idea is to study the effect of educational campaigns with a vaccination treatment in practical Ebola situations. The case of the French nurse cured of Ebola is a proof of the possibility of educational campaigns and treatment [32]. An educational campaign, in case of spread of Ebola, has great importance. In fact, Ebola virus spreads through human-to-human transmission, not only by close and direct physical contact with infected bodily fluids, but also via exposure to objects or contaminated environment. The most infectious fluids are blood, feces, and vomit secretions. However, all body fluids have the capacity to transmit the virus. Here, we intend to control the propagation of the Ebola virus by using two control variables in the SEIR model, as follows:

$$\begin{cases} \frac{dS(t)}{dt} = -\beta S(t)I(t) - u_2(t)S(t), \\ \frac{dE(t)}{dt} = \beta S(t)I(t) - \gamma E(t), \\ \frac{dI(t)}{dt} = \gamma E(t) - \mu I(t) - u_1(t)I(t), \\ \frac{dR(t)}{dt} = \mu I(t) + u_1(t)I(t) + u_2(t)S(t), \end{cases} \quad (6)$$

where $u_1(t)$ is the fraction of infective that is treated at time t , and $u_2(t)$ is the fraction of susceptible individuals that is subject to an educational campaign at time t . Our goal is to minimize simultaneously the total number of individuals that are infected, the cost of treatment, and the cost of educational campaigns

to the population. The objective functional is now

$$J(u) = \int_0^{t_{end}} \left[\kappa I(t) + B_1 \frac{u_1^2(t)}{2} + B_2 \frac{u_2^2(t)}{2} \right] dt \quad (7)$$

subject to system (6), where $u = (u_1, u_2)$, with u_1 representing treatment and u_2 educational campaigns, and κ , B_1 and B_2 are weight parameters. The Lebesgue measurable control set is defined as

$$\mathcal{U}_{ad} := \{u = (u_1, u_2) : u \in L^1, 0 \leq u_1(t), u_2(t) \leq u_{\max}, t \in [0, t_{end}]\},$$

where $u_{\max} = 0.9$. We choose quadratic terms with respect to the controls in order to describe the nonlinear behaviour of the cost of implementing the educational campaign and treatments. The first term in the objective functional (7), κI , stands for the total number of individuals that are infected; the term $B_1 u_1^2/2$ represents the cost of treatment; while the term $B_2 u_2^2/2$ represents the cost associated with the educational campaign. Figure 7 shows the time-dependent curve of susceptible individuals, $S(t)$, which decreases more rapidly in case of the optimal control with Strategy 3. It reaches 1% at the end of the campaign, instead of 6.6% at the end of the campaign in case of Strategy 1, and against 17.3% in the absence of optimal control. Figure 8 shows that the number of recovered individuals of Strategy 3 increases rapidly until 98.9%, instead of 93.3% in case of Strategy 1, and against 81.2% without control. Figure 9 shows that the number of exposed individuals of Strategy 3 increases the most rapidly. The period of incubation of the virus is the least important (30 days) instead of 60 days in case of Strategy 1. In Figure 10 we see the time-dependent curve of infected individuals $I(t)$, which decreases mostly. The other important effect of the Strategy 3, which we can see in the same curve, is the period of infection, which is the less important. The value of the period of infection is 30 days in case of Strategy 3, instead of 80 days in case of Strategy 1, and against 100 days without vaccination. This shows the efficiency of the effect of educational campaigns in controlling Ebola virus with the vaccination control treatment described in Strategy 3. Figure 11 gives a representation of the optimal control variables $u_1(t)$ and $u_2(t)$ of Strategy 3. The minimum of the $J(u)$ functional (7) of Strategy 3 is 0.94.

4 Discussion

In this section we compare between the three strategies of Section 3, and we discuss the obtained results. Figures 12 and 13 represent, respectively, the time-dependent curve of susceptible S and recovered individuals R . The curves of S and R of Strategy 3 are slightly greater than the curves of S and R of Strategy 2, which is logical because in the cost functional of Strategy 2 we minimize the infected and the exposed individuals with vaccination, where in the cost functional of Strategy 3 we minimize the infected number with the cost of educational campaigns and vaccination. It is important in the comparison

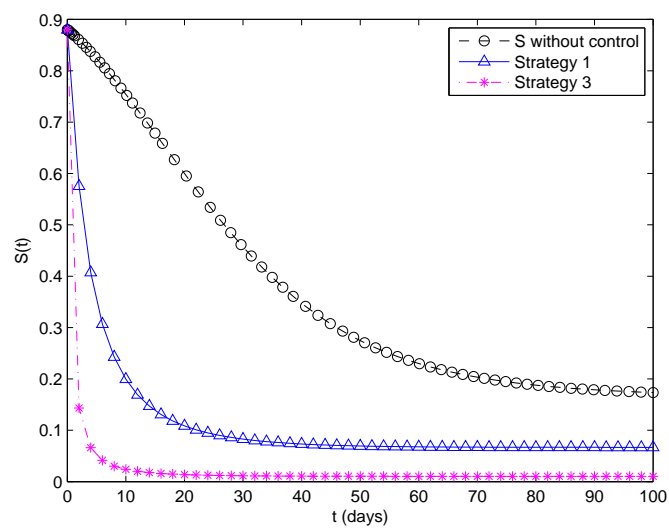


Fig. 7 Comparison between the curves of susceptible individuals $S(t)$ in case of Strategy 1 and Strategy 3 *versus* without control.

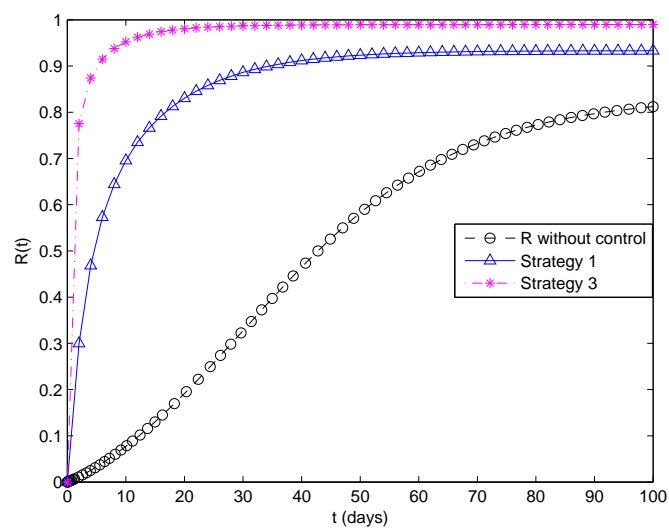


Fig. 8 Comparison between the curves of recovered individuals $R(t)$ in case of Strategy 1 and Strategy 3 *versus* without control.

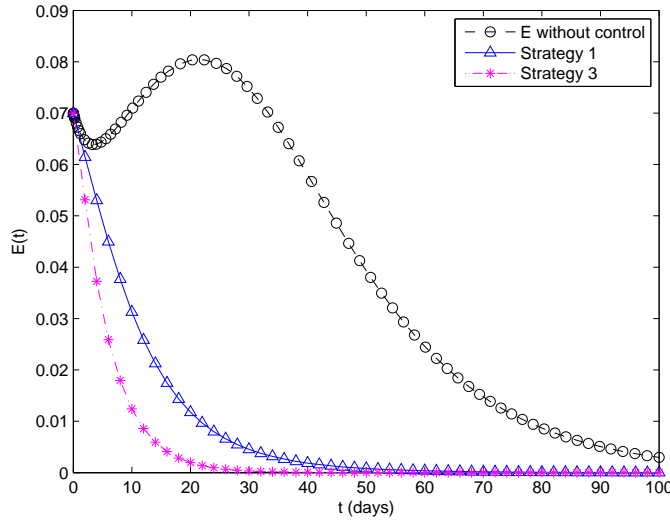


Fig. 9 Comparison between the curves of exposed individuals $E(t)$ in case of Strategy 1 and Strategy 3 *versus* without control.

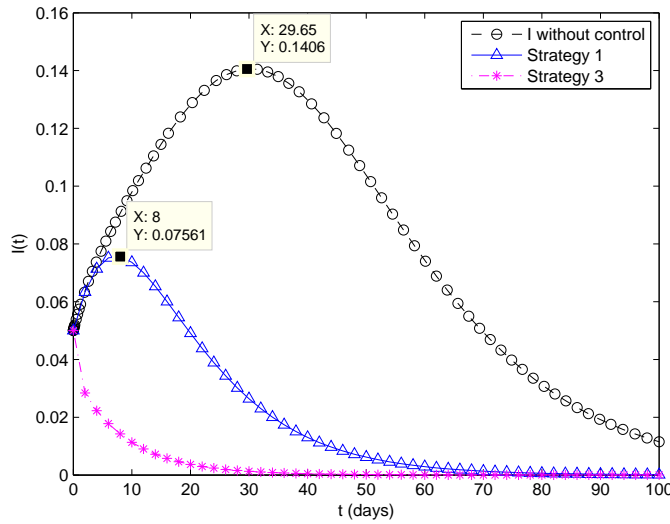


Fig. 10 Comparison between the curves of infected individuals $I(t)$ in case of Strategy 1 and Strategy 3 *versus* without control.

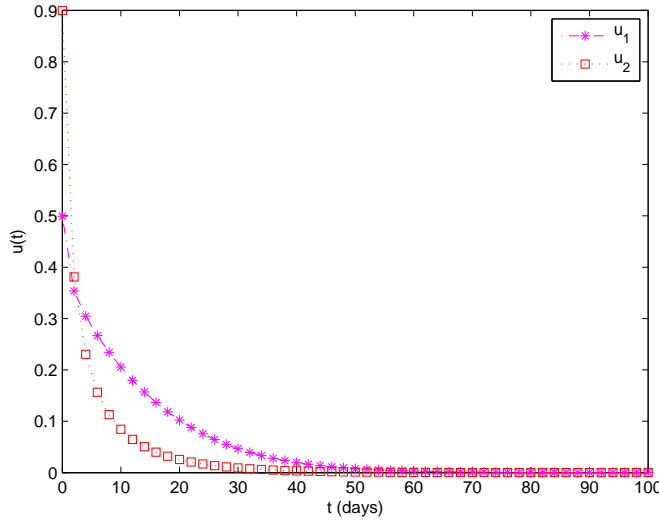


Fig. 11 The optimal control variables u_1 and u_2 for Strategy 3.

between the three curves to note that the number of exposed and infected individuals decrease the most rapidly in case of Strategy 3 (see Figures 14 and 15). Moreover, there is not any peak in case of Strategy 3. The results show the efficiency of an educational campaign in controlling Ebola virus when we couple it with the vaccination treatment control (as given in Strategy 3). We conclude that one can improve vaccination by educational campaigns, which has a great importance in poor countries who do not have the capacity to defend themselves against the virus.

5 Conclusion

We studied several optimal control problems for the SEIR model recently discussed by Rachah and Torres in [22], which provides a good description of the 2014 Ebola outbreak in West Africa. Precisely, we introduced a control $u(t)$ representing the vaccination rate at time t (Section 3.1). Then we addressed the problem of reducing not only the number of infected individuals $I(t)$ but also the number of exposed individuals $E(t)$ (Section 3.2). Finally, we investigated the integration of an educational campaign about the virus into the population (Section 3.3). It has been shown that an educational campaign has a great importance with the vaccination treatment, mainly in countries that do not have the capacity to defend themselves against the virus. As future work, we plan to include in our study other factors. For instance, we intend to include in the mathematical model a quarantine procedure.

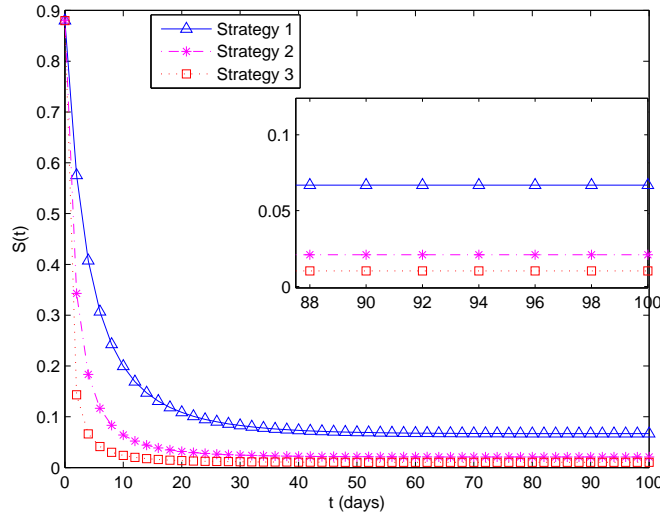


Fig. 12 Comparison between the curves of susceptible individuals $S(t)$ in case of Strategy 1, Strategy 2, and Strategy 3.

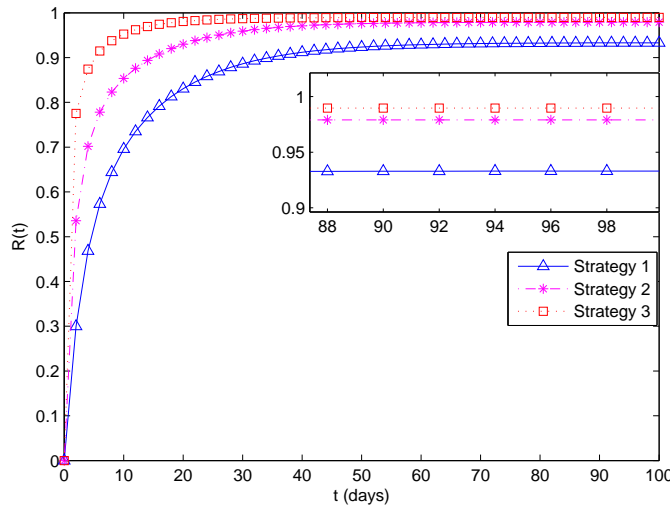


Fig. 13 Comparison between the curves of recovered individuals $R(t)$ in case of Strategy 1, Strategy 2, and Strategy 3.

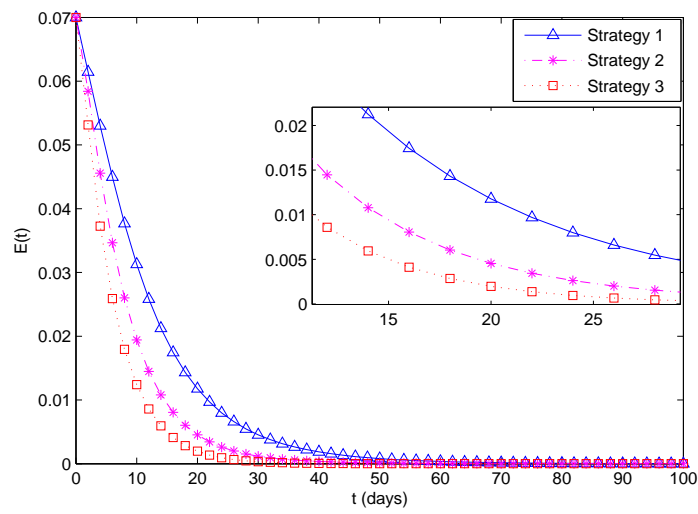


Fig. 14 Comparison between the curves of exposed individuals $E(t)$ in case of Strategy 1, Strategy 2, and Strategy 3.

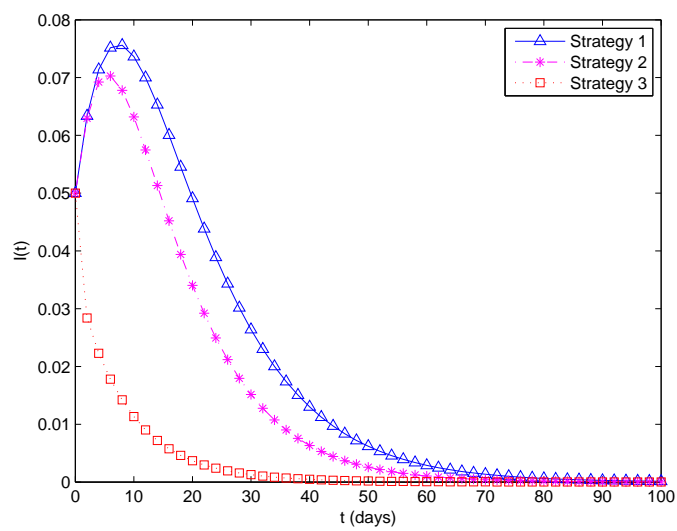


Fig. 15 Comparison between the curves of infected individuals $I(t)$ in case of Strategy 1, Strategy 2, and Strategy 3.

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